Packaging, storage, and disposal options to enhance opioid safety: Target Problems and Labeling Considerations

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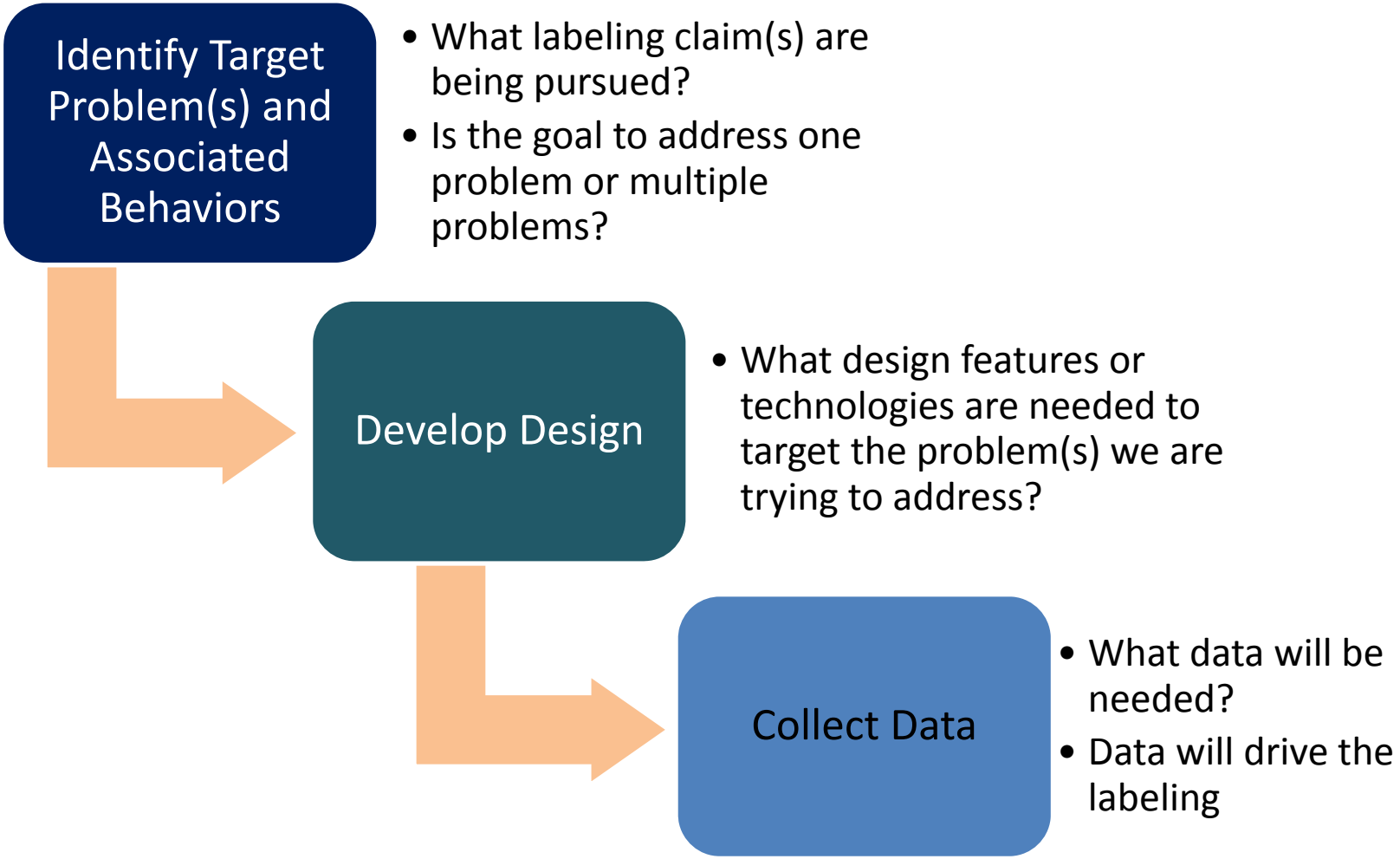
Overview

- Accidental Exposure
- Misuse
- Third Party Access
- Excess Supply

Approach to Development




Accidental Exposure
Excess Supply
Identifying Problems
Misuse
Third Party Access

Accidental Exposure

Accidental Exposure

‘The Pills Are Everywhere’: How the Opioid Crisis Claims Its Youngest Victims

By JULIE TURKEWITZ SEPT. 20, 2017

When Penny Mae Cormani died in Utah, her family sang Mormon hymns — “Be Still My Soul” — and lowered her small coffin into the earth. The latest victim of a drug epidemic that is now taking 60,000 lives a year, Penny was just 1.

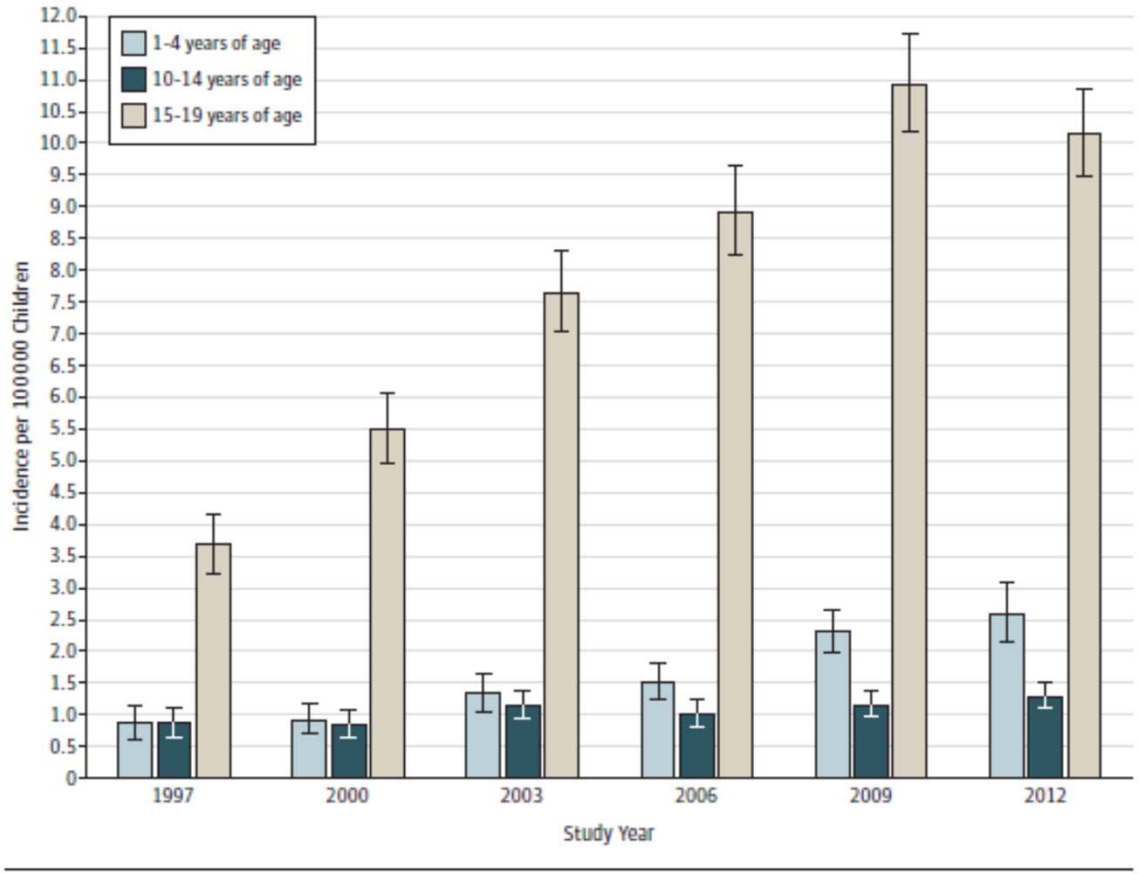
Increasingly, parents and the police are encountering toddlers and young children unconscious or dead after consuming an adult’s opioids.

“These kids aren’t making a choice because they are trying to get high on a substance. It’s that the pills are everywhere.”

The New York Times, Sept 20, 2017, https://www.nytimes.com/2017/09/20/us/opioid-deaths-children.html
Image: Asociación Española de Pediatría, http://enfamilia.aeped.es/temas-salud/intoxicaciones-por-medicamentos-en-ninos

Accidental Exposure

Figure 1. Weighted National Estimates of Temporal Trends in Hospitalizations for Prescription Opioid Poisonings Stratified by Age Category

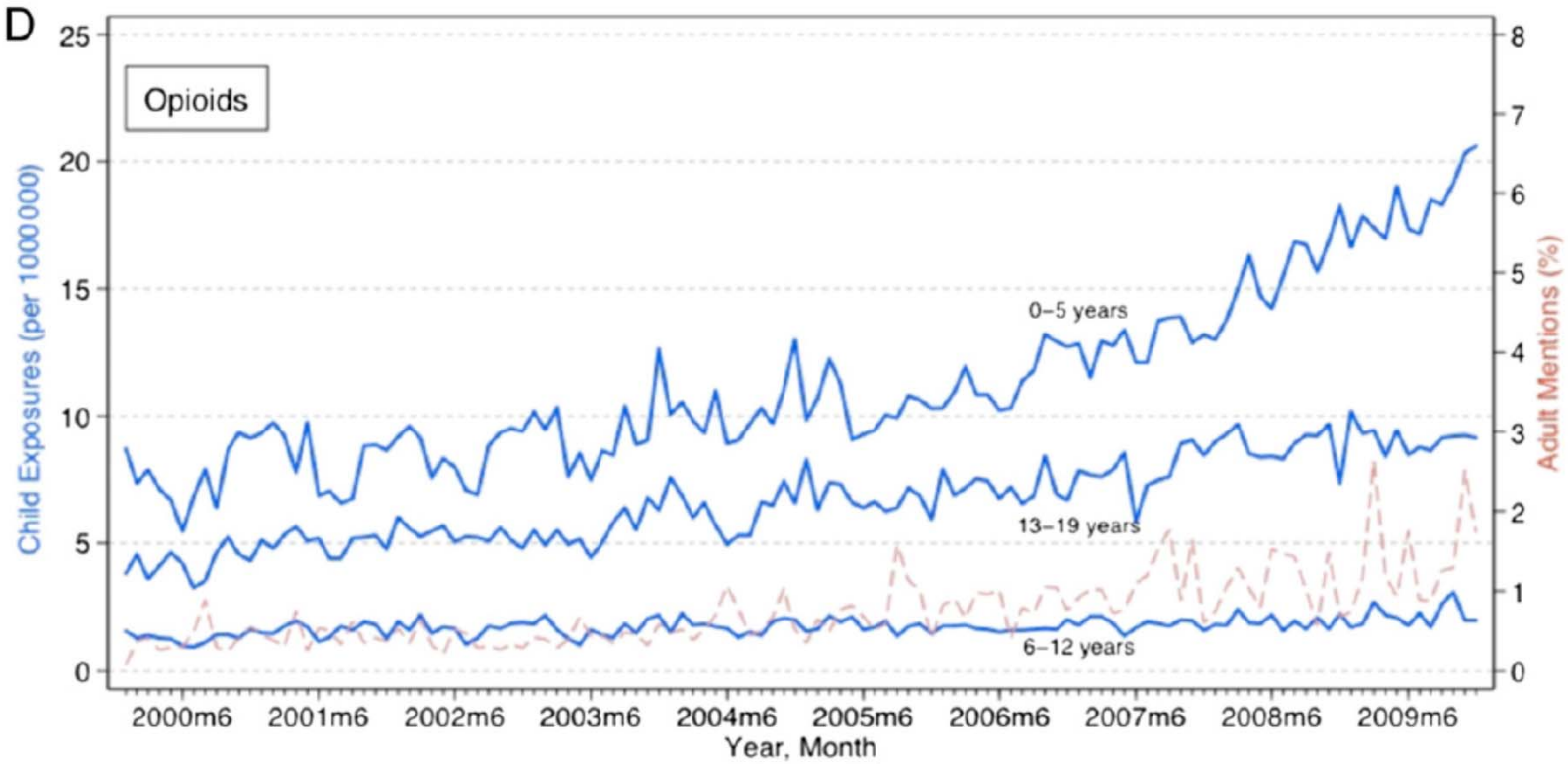


Error bars indicate 95% CI (*P* for trend, <.001 for all ages). Estimates for 5- to 9-year-olds do not meet the criteria for statistical reliability and thus are not shown.

Findings: "This retrospective analysis of 13,052 national hospital discharge records found that pediatric hospitalizations for opioid poisonings increased nearly 2-fold from 1997 to 2012. Hospitalization rates were highest in older adolescents, but the largest percentage increase in hospitalizations over time occurred among the youngest children (toddlers and preschoolers)"

Gaither J et al. *JAMA Pediatrics* 2016; 170(12):1195-1201

Accidental Exposure



There were significant associations between adult medication use and exposures and poisonings in children…These associations were generally twice as strong for opioids as other drug classes and strongest among children 0 to 5 years of age across drug classes.

Burghardt LC et al. *Pediatrics* 2013; 132:18-27

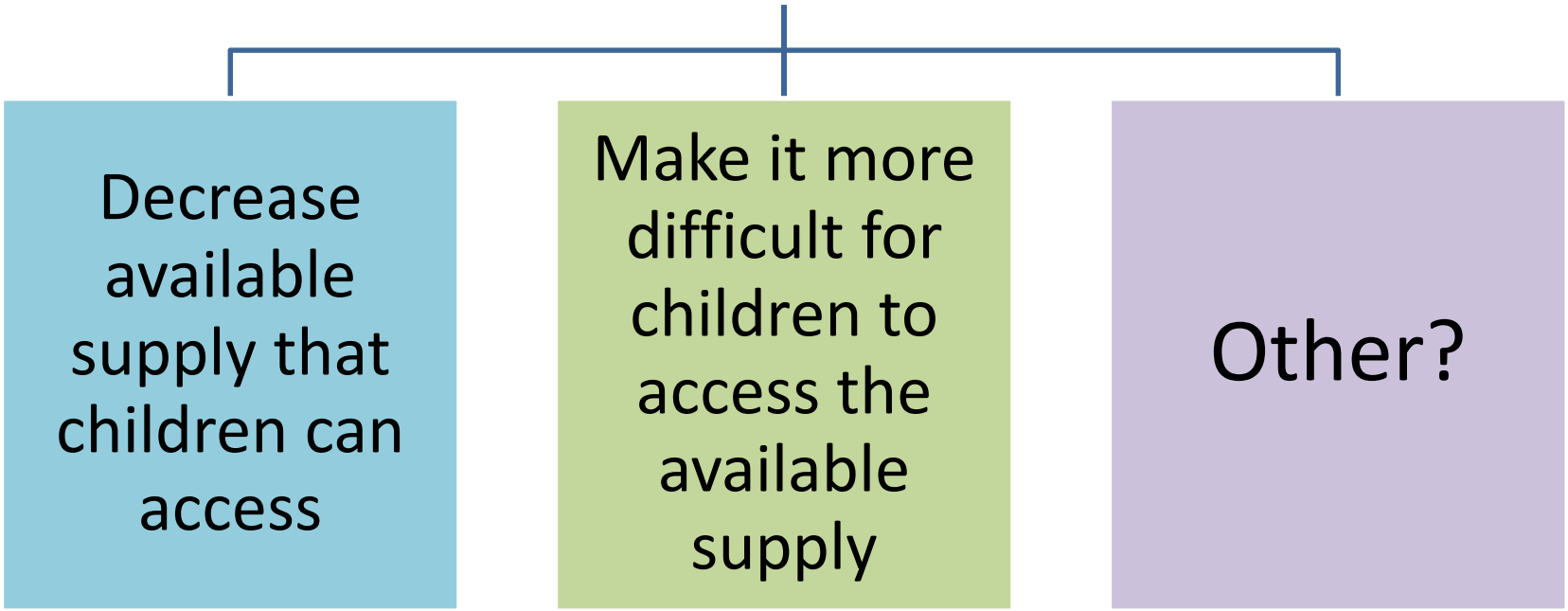
Accidental Exposure

Why do accidental ingestions continue to occur?

- Improper use of child-resistant closures
  - Leaving container open
  - Incompletely closing container
  - Transferring contents of one bottle to another container
- Availability of non-special packaging, on request, for prescription medication
- Inadequate quality control by manufacturers leading to defective closures
- Violations of the law by the pharmacist and/or the dispensing physician

Accidental Exposure

Where might we focus interventions?



Accidental Exposure

- Example
  - Parent leaves bottle of XXX on table or counter and has not properly twisted the cap back on. Toddler finds the bottle and easily opens the top and eats the medicine. Toddler is subsequently hospitalized for massive overdose of XXX.
- Labeling Considerations*
  - *The packaging has characteristics expected to lower the risk for accidental pediatric exposure of XXX. However, pediatric accidental exposure of XXX is still possible.*

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Misuse

Misuse

Comprehensive Review

PAIN

Rates of opioid misuse, abuse, and addiction in chronic pain: a systematic review and data synthesis

Kevin E. Vowles[a,*], Mindy L. McEntee[a], Peter Siyahhan Julnes[a], Tessa Frohe[a], John P. Ney[b], David N. van der Goes[c]

Abstract

Opioid use in chronic pain treatment is complex, as patients may derive both benefit *and* harm. Identification of individuals currently using opioids in a problematic way is important given the substantial recent increases in prescription rates and consequent increases in morbidity and mortality. The present review provides updated and expanded information regarding rates of problematic opioid use in chronic pain. Because previous reviews have indicated substantial variability in this literature, several steps were taken to enhance precision and utility. First, problematic use was coded using explicitly defined terms, referring to different patterns of use (ie, misuse, abuse, and addiction). Second, average prevalence rates were calculated and weighted by sample size and study quality. Third, the influence of differences in study methodology was examined. In total, data from 38 studies were included. Rates of problematic use were quite broad, ranging from <1% to 81% across studies. Across most calculations, rates of misuse averaged between 21% and 29% (range, 95% confidence interval [CI]: 13%-38%). Rates of addiction averaged between 8% and 12% (range, 95% CI: 3%-17%). Abuse was reported in only a single study. Only 1 difference emerged when study methods were examined, where rates of addiction were lower in studies that identified prevalence assessment as a primary, rather than secondary, objective. Although significant variability remains in this literature, this review provides guidance regarding possible average rates of opioid misuse and addiction and also highlights areas in need of further clarification.

Keywords: Opioids, Chronic pain, Problematic use, Abuse, Addiction, Misuse

"Roughly 21 to 29 percent of patients prescribed opioids for chronic pain misuse them."

Vowles KE et al. *PAIN* 2015; 156(4): 569-576

National Institute on Drug Abuse (NIDA) https://www.drugabuse.gov/drugs-abuse/opioids/opioid-overdose-crisis#six

Image: Liga da Saúde, https://ligadasaude.blogspot.com/2012/09/idosos-podem-estar-usando-medicamentos.html

Misuse

Each day more than 1,000 people are treated in emergency departments for not using prescription opioids as directed

The DAWN Report. Rockville, MD: US Department of Health and Human Services, Substance Abuse and Mental Health Services Administration; 2013.
Image: The University of Texas at Austin, http://www.texasenterprise.utexas.edu/2013/10/10/innovation/reinventing-er-hospital-takes-cues-assembly-lines

Misuse

Unintended Misuse*

- Example
  - Patient forgets to take medication
  - Patient doesn't understand how often to take medication

Intended Misuse

- Example
  - Therapeutic use of drug by a person other than the intended patient that may result from sharing of medication (e.g., giving a friend a Vicodin tablet for her migraine)
  - Intended patient uses more drug than prescribed to self-treat increasing or breakthrough pain
  - Intended patient retains leftover opioid in case of future pain (contributing to excess available supply which could potentially be accessed by a third party)

*The use of the term "**unintentional** misuse" in this context is not to be confused with the definition of misuse as the **intentional** therapeutic use of a drug product in an inappropriate way that specifically excludes the definition of abuse

Misuse

- Could contribute to accidental overdose of an opioid
- Could be a sign of developing addiction
- Could contribute to excess available supply that is susceptible to access by a third party
- Could contribute to individuals not seeking necessary care from a healthcare provider

Misuse

- Labeling Considerations*
  - *The packaging has characteristics that improve patient compliance with labeled directions for use.*
  - *The packaging has characteristics that will destroy XXX after ## days of use, eliminating excess supply of XXX.*
  - *The packaging has characteristics expected to discourage the sharing of XXX.*

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Third Party Access - Outpatient

Third Party Access

Published in final edited form as:
J Pediatr. 2015 September ; 167(3): 605–12.e1-2. doi:10.1016/j.jpeds.2015.04.071.

Nonmedical Prescription Opioid Use in Childhood and Early Adolescence Predicts Transitions to Heroin Use in Young Adulthood: A National Study

Magdalena Cerdá, DrPH, MPH[1,2], Julián Santaella, DVM, MSc[1], Brandon D. L. Marshall, PhD[3], June H. Kim, MHS[1], and **Silvia S. Martins, MD, PhD[1]**

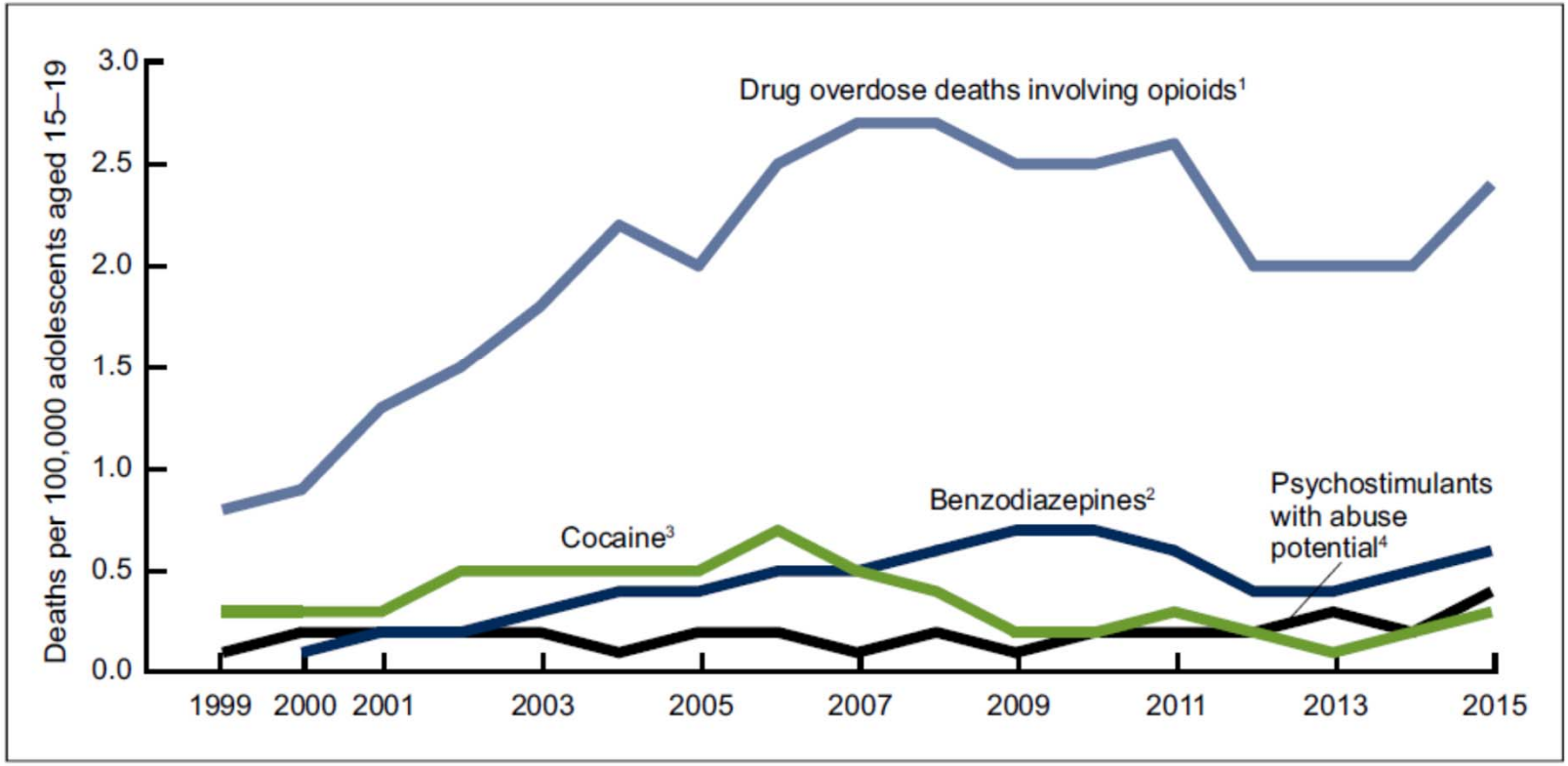
"Primary prevention of nonmedical use of prescription opioids in late childhood may prevent the onset of more severe types of drug use such as heroin at later ages."

Cerdá M et al. *J Pediatr*. 2015; 167(3): 605-612

Image: Choose Help, https://www.choosehelp.com/blogs/prescription-drug-abuse/teen-campaign-against-deadly-abuse-of-prescription-drugs.html

Third Party Access

Figure 3. Drug overdose death rates for adolescents aged 15–19, by type of drug involved: United States, 1999–2015



NCHS Data Brief No. 282, August 2017

Third Party Access - Inpatient

Annals of Internal Medicine | ORIGINAL RESEARCH

Health Care–Associated Hepatitis C Virus Infections Attributed to Narcotic Diversion

Walter C. Hellinger, MD; Laura P. Bacalis, RN; Robyn S. Kay, MPH; Nicola D. Thompson, PhD, MS; Guo-Liang Xia, MD, MPH; Yulin Lin, MD; Yury E. Khudyakov, PhD; and Joseph F. Perz, DrPH

Background: Three cases of genetically related hepatitis C virus (HCV) infection that were unattributable to infection control breaches were identified at a health care facility.

Objective: To investigate HCV transmission from an HCV-infected health care worker to patients through drug diversion.

Design: Cluster and look-back investigations.

Setting: Acute care hospital and affiliated multispecialty clinic.

Patients: Inpatients and outpatients during the period of HCV transmission.

Measurements: Employee work and narcotic dispensing records, blood testing for HCV antibody and RNA, and sequencing of the *NS5B* gene and the hypervariable region 1 of the *E2* gene.

Results: 21 employees were recorded as being at work or as retrieving a narcotic from an automated dispensing cabinet in an area where a narcotic was administered to each of the 3 case patients; all employees provided blood samples for HCV testing. One employee was infected with HCV that had more than 95% *NS5B* sequence homology with the HCV strains of the 3 case patients. Quasi-species analysis showed close genetic relatedness with variants from each of the case patients and more than 97.9% nucleotide identity. The employee acknowledged parenteral opiate diversion. An investigation identified 6132 patients at risk for exposure to HCV because of the drug diversion. Of the 3929 living patients, 3444 (87.7%) were screened for infection. Two additional cases of genetically related HCV infection attributable to the employee were identified.

Limitation: Of the living patients at risk for HCV exposure, 12.3% were not tested.

Conclusion: Five cases of HCV infection occurring over 3 to 4 years were attributed to drug diversion by an HCV-infected health care worker. Studies of drug diversion and assessments of strategies to prevent narcotics tampering in all health care settings are needed.

Primary Funding Source: None.

Ann Intern Med. 2012;156:477-482. www.annals.org
For author affiliations, see end of text.

Third Party Access - Inpatient

Image: Rx-wiki, http://rx-wiki.org/index.php?title=File:AcuDose-RxLargeMainCabinetSideView-hires.jpg
Image: Outpatient Surgery Magazine, http://www.outpatientsurgery.net/surgical-facility-administration/legal-and-regulatory/colorado-nurse-indicted-for-pain-med-theft--e-06-09-09
Image: Opiate Addiction & Treatment Resource, http://www.opiateaddictionresource.com/media/images/fentanyl_iv

Third Party Access

- Example
  - Outpatient
    - Adolescents in a household who might be curious or experimenting with opioids
  - Inpatient
    - Healthcare professional withdraws injectable opioid product from vial for self administration and replaces the removed content with saline
- Labeling Considerations*
  - *The packaging has characteristics expected to reduce use by persons other than the intended patient.*

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Excess Supply

Journal of Adolescent Health 52 (2013) 480–485

ELSEVIER

JOURNAL OF ADOLESCENT HEALTH
www.jahonline.org

Original article

Leftover Prescription Opioids and Nonmedical Use Among High School Seniors: A Multi-Cohort National Study

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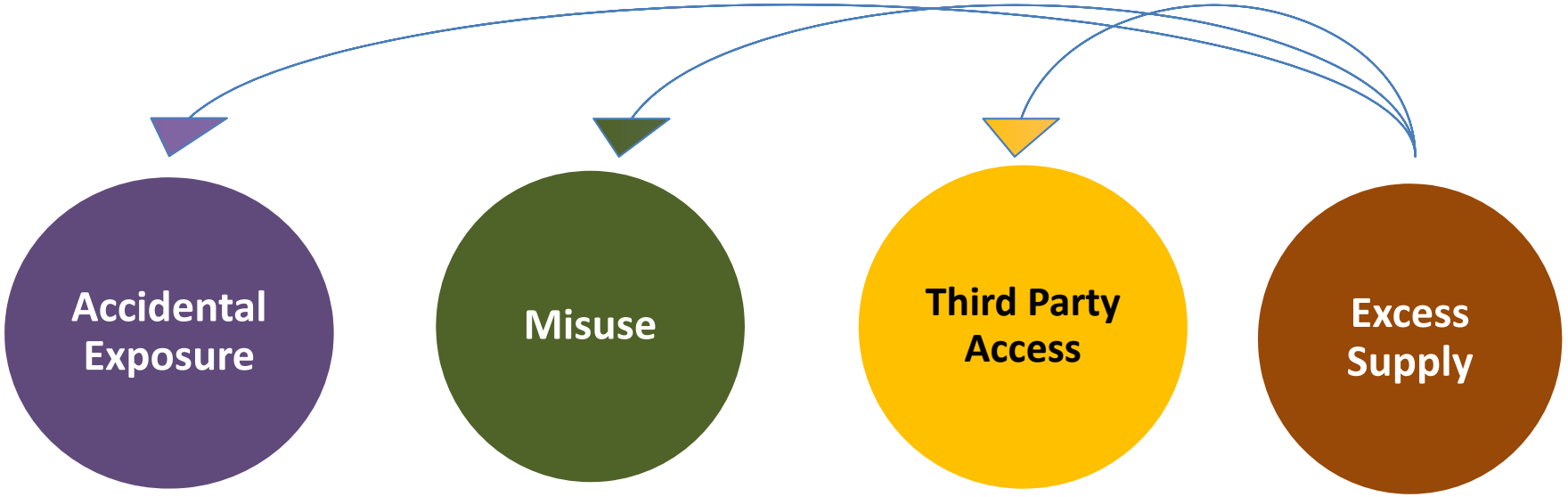
Article history: Received April 9, 2012; Accepted August 21, 2012
Keywords: Epidemiology; Adolescents; Prescription opioids; Nonmedical use; Diversion; Adolescents; Medication; Substance use; High school

"…leftover prescription opioids from previous prescriptions account for a substantial source of [nonmedical use of prescription opioids] among high school seniors in the U.S."

McCabe SE et al. *J Adolesc Health* 2013; 52(4): 480-5
Image: GeriPal, http://www.geripal.org/2013/08/inappropriate-management-of.html

Excess Supply



Several Small Studies Have Assessed Leftover Pills, Storage, and Disposal After Surgery

Weeks Later

- Asked the patient:
  - How many pills used/remaining
  - Whether they disposed of excess opioid medication
  - How/where they stored excess supply

Opioid Prescribing: Surgical Procedures

Procedure	Mean (range) tablets filled	Mean tablets consumed	Mean tablets remaining
Laparoscopic Inguinal Hernia Repair	33 (15-70)	9	23
Open Inguinal Hernia Repair	30 (15-120)	9	21
Laparoscopic Cholecystectomy	30 (0-100)	10	20
Cesarean Delivery	40 (5-80)*	20*	15*
Partial Mastectomy	21 (0-50)	3	18
Partial Mastectomy with Node Biopsy	23 (0-60)	6	17
Tooth Extraction	28 (n.d.)	13	17
Dermatologic Surgery	9 (3-20)	4	5
Orthopedic Surgery	80 (n.d.)	n.d.	30
Upper Extremity Surgery	30 (n.d.)	14 (Bone) 9 (Soft Tissue)	19
Outpatient Shoulder Surgery	55 (n.d.)	n.d.	20

*** Median number of pills**

Sources: Hill, et al., *Ann Surg*, 2017; Bateman, et al., *Obstet Gyn*, 2017; Maughan, et al., *Drug Alc Dep*, 2016,; Harris, et al., *JAMA Dermatol*. 2013; Bockman, et al. *J Pain, 2017* (Abstract); Rogers, et al., *J Hand Surg*, 2012; Kumar, et al. *AJSM*, 2017

Excess Supply

- Example
  - Patient does not use all of his prescribed medication and leaves the leftover medication in the medicine cabinet. Subsequently, _____finds the excess supply of XXX.
- Labeling Considerations*
  - *The packaging has characteristics that will destroy XXX after ## days of use, eliminating excess supply of XXX.*

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